Remarks/Arguments

The foregoing amendments to the claims are of formal nature, and do not add new matter. Prior to the present amendment, claims 39-44 were pending in this application and were rejected on various grounds. Claim 44 has been canceled without prejudice and claim 39 has been amended. The rejection to the presently pending claims are respectfully traversed.

Sequence Compliance

Applicants gratefully acknowledge the Examiner's remarks that sequence compliance in the instant application has been fulfilled.

Formal Drawings

Formal drawings with the correct margins are attached herewith.

Oath/Declaration

According to the Office Action, the oath or declaration is defective, and a new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. In explaining the requirement, the Examiner noted that the oath or declaration is defective "because: non-initialed and non-dated alterations have been made to the oath or declaration." Accordingly, a new declaration, duly signed by Wei-Qiang Gao, is herewith attached.

Priority

(5A) The Examiner has concluded that Applicants are entitled only to the priority of US Application No. 09/902,713, filed July 10, 2001, because the subject matter of the present application "is not supported by any of the others because the instant subject matter lacks the necessary support under 35 USC 112, first paragraph. As it will be apparent from the rest of the response, Applicants rely on the gene amplification results (Example 92) to establish substantial and specific asserted utility for the polypeptide PRO269 and the antibodies that it binds. These

results were first disclosed in international application PCT/US00/03565 (P2931R1), filed on February 11, 2000, and published as WO 01/53486 on July 26, 2001 (Pages 138-191 (Example 26), specifically at page 183 and in Table 7, pages 152-163). Accordingly, the effective filing date of this application is February 11, 2000.

(5B) The current amendment to the specification to include the indication that the international applications to which the present application claims benefit were published in English under PCT Article 21(2) and to include the status of non-provisional parent application(s) in the priority claim is believed to overcome the present objection.

IDS

The supplemental IDS in compliance with provisions of 37 CFR 1.97 and 1.98 submitted herewith is believed to overcome the present objection.

Title

The current amendment to the title to read "ANTIBODIES TO PRO269 POLYPEPTIDES" is believed to overcome the present objection to the title.

Specification

8) The specification has been objected to for containing an embedded hyperlink. The foregoing amendment, which deleted all embedded hyperlinks or other forms of browser executable code, is believed to overcome this objection.

9) The specification has been amended to reflect the changed address for ATCC and is believed to overcome this objection.

In addition, amendments to the specification have incorporated the requisite assurances that "all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of the pertinent U.S. patent."

Claim Objection

Claim 43 was objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, claim 39. The Examiner objected to the claim since it allegedly encompassed a labeled antibody that did not appear in the specification which thus, broadens rather than narrows the claim. Applicants respectfully traverse.

Support for "labeled antibody" is found in the specification on page 77, lines 9-12 and thus claim 43 satisfies the conditions of 37 CFR 1.75(c). Accordingly, Applicants request that this objection be withdrawn.

35 USC § 101

Claims 39-44 were rejected under 35 U.S.C. 101 "because the claimed invention is not supported by either a credible, specific and substantial asserted utility or a well established utility." The Examiner specifically noted that "....utility for purification of a protein (and other asserted utilities) requires that the protein itself have a specific and substantial or well established utility." The Examiner specifically cited Brenner v. Manson as stating that "Congress intended that no patent be granted on a chemical compound whose sole 'utility' consists of its potential role as an object of use-testing."

The rejection is respectfully traversed.

Utility - Legal Standard

According to the Utility Examination Guidelines ("Utility Guidelines"), 66 Fed. Reg. 1092 (2001) an invention complies with the utility requirement of 35 U.S.C. § 101, if it has at least one asserted "specific, substantial, and credible utility" or a "well-established utility." Under the Utility Guidelines, a utility is "specific" when it is particular to the subject matter claimed. For example, it is generally not enough to state that a nucleic acid is useful as a diagnostic without also identifying the conditions that is to be diagnosed.

The requirement of "substantial utility" defines a "real world" use, and derives from the Supreme Court's holding in *Brenner v. Manson*, 383 U.S. 519, 534 (1966) stating that "The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility." In. explaining the

"substantial utility" standard, M.P.E.P. 2107.01 cautions, however, that Office personnel must be careful not to interpret the phrase "immediate benefit to the public" or similar formulations used in certain court decisions to mean that products or services based on the claimed invention must be "currently available" to the public in order to satisfy the utility requirement. "Rather, **any reasonable use that an applicant has identified for the invention that can be viewed as providing a public benefit should be accepted as sufficient**, at least with regard to defining a "substantial" utility." (M.P.E.P. 2107.01, emphasis added.) Indeed, the Guidelines for Examination of Applications for Compliance With the Utility Requirement, set forth in M.P.E.P, 2107 II (B) (1) gives the following instruction to patent examiners: "If the applicant has asserted that the claimed invention is useful for any particular practical purpose ... and the assertion would be considered credible by a person of ordinary skill in the art, do not impose a rejection based on lack of utility."

Finally, the Utility Guidelines restate the Patent Office's long established position that any asserted utility has to be "credible." "Credibility is assessed from the perspective of one of ordinary skill in the art in view of the disclosure and any other evidence of record ... that is probative of the applicant's assertions." (M.P.E.P. 2107 II (B) (1) (ii)) Such standard is presumptively satisfied unless the logic underlying the assertion is seriously flawed, or if the facts upon which the assertion is based are inconsistent with the logic underlying the assertion (Revised Interim Utility Guidelines Training Materials, 1999).

Proper Application of the Legal Standard

Applicants submit that the gene amplification data provided in the present application and as explained below are sufficient to establish a specific, substantial and credible utility for the PRO269 polypeptide to which the claimed antibodies are directed.

Gene amplification is an essential mechanism for oncogene activation. This data was first disclosed in international application PCT/US00/03565 (P2931R1), filed on February 11, 2000, and published as WO 01/53486 on July 26, 2001.

It is well known that gene amplification occurs in most solid tumors, and generally is associated with poor prognosis. As described in Example 92 of the present application, the inventors isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 9 (pages 229-234 of the specification), including primary lung cancers of the type and stage indicated in Table 8 (page 227). As a negative control, DNA was isolated from the cells of ten normal healthy individuals, which was pooled and used as a control (page 222, lines 34-36). Gene amplification was monitored using real-time quantitative TaqMan™ PCR. The gene amplification results are set forth in Table 9. As explained in the passage bridging pages 222 and 223, the results of TaqMan™ PCR are reported in ΔCt units. One unit corresponds to one PCR cycle or approximately a 2-fold amplification, relative to control, two units correspond to 4-fold, 3 units to 8-fold, etc. amplification. PRO269 showed approximately 2-3-fold amplification in 8 primary lung tumors. Accordingly, antagonist antibodies to PRO269 polypeptides can be a useful diagnostic reagent for diagnosing lung tumors.

The attached Declaration by Audrey Goddard clearly establishes that the TaqMan™ realtime PCR method described in Example 92 has gained wide recognition for its versatility, sensitivity and accuracy, and is in extensive use for the study of gene amplification. The Declaration also confirms that based upon the gene amplification results set forth in Table 9 one of ordinary skill would find it credible that PRO269 is a diagnostic marker of human lung cancer. It is, of course, true that further research might be needed to develop PRO269 into a diagnostic product. However, the fact that such follow-up tests might be necessary, cannot properly lead to the legal conclusion that PRO269 lacks patentable utility.

As set forth in M.P.E.P, 2107 II (B) (1), if the applicant has asserted that the claimed invention is useful for any particular practical purpose, and the assertion would be considered credible by a person of ordinary skill in the art, a rejection based on lack of utility should not be imposed. The attached Declaration by Audrey Goddard establishes that the asserted utility in viewed "credible" by one skilled in the art. Indeed, the logic underlying Applicants' assertion that PRO269 is a diagnostic marker of lung cancer cannot be viewed as "seriously flawed," and the facts upon which the assertion is based are not inconsistent with the logic underlying the

assertion. It is always possible that an invention fails on its way of development to a commercial product. Thus, despite recent advances in rational drug design, a large percentage of drug candidates fails, and never makes it into a drug product. However, the USPTO is not the FDA, the law does not require that a product (drug or diagnostic) be currently available to the public in order to satisfy the utility requirement.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

35 USC § 112, First Paragraph/Enablement

13,14) Claims 39-44 have been rejected under 35 USC §112, first paragraph because allegedly "the claimed invention is not supported by either a credible specific and substantial asserted utility, hence one skilled in the art clearly would not know how to use the claimed invention." Further, the Examiner noted that "even if the antibody were enabled, ...the connection between these in vitro activities and any particular disease is unclear."

In response to the previous rejection under 35 U.S.C. 101, Applicants have shown that the specification discloses a substantial, specific and credible utility using the gene amplification data for the PRO269 polypeptides. Applicants showed that PRO269 showed approximately 2-3-fold amplification in "8 primary lung tumors" and hence, there is a correlation between the disclosed polypeptides and lung tumors, as discussed above. Accordingly, antagonist antibodies to PRO269 polypeptides can be useful for diagnosing lung tumors. Applicants submit that, taken with the knowledge present in the art at the effective priority date of this application, one skilled in the art was able to practice the claimed invention without undue experimentation.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the rejection of all pending claims under this section.

35 USC § 112, Second Paragraph

Claims 39-44 have been rejected under 35 USC § 112, second paragraph as "indefinite." The Examiner noted that, regarding claims 39 and 44, the recitation of 'specific binding' is not clear.

Cancellation of claim 44 without prejudice and the present amendment to claim 39 is believed to overcome this rejection.

35 USC § 102 and 103

(20) Claims 39-44 were rejected under 35 U.S.C. 102(b), or in the alternative under 35 U.S.C. 102(a) "as being anticipated by Wood et al. (WO 99/14328), see pages 1, 12, 39, 56, 72, 83-85, 92-98, 101, 108-112, 126-127, 185-187, Figures 35 and 36, as evidenced by the attached alignment 'D'."

The publication date of the Wood et al. reference (WO 99/14328) is March 25, 1999. As presented above, PCT/US00/03565 (P2931R1), filed on February 11, 2000, duly disclosed the overexpression of PRO269 polypeptides in lung tumor, against which the claimed antibodies are directed. Accordingly, all claims pending in this application are entitled to the February 11, 2000 priority date, and the cited reference is not available as prior art under either 35 USC 102(b).

Wood et al. is not a valid reference under 35 USC 102(a) either. In *In re Wilder*, the court acknowledged that an application claiming a certain compound could avoid the anticipatory effect of a prior publication specifically naming the same compound by showing that the claimed compound has "properties completely different from those attributed to them by the reference description." 429 F.2d 447, 451, 166 USPQ 545 (C.C.P.A. 1970). Wood et al. describes the PRO269 polypeptide as a newly identified member of the thrombomodulin family, which therefore may be useful as an antithrombotic agent. In contrast, the present invention identified PRO269 polypeptides as a marker of lung cancer. Accordingly, the claimed antibodies have uses as diagnostic agents for lung cancer. Since the properties of the claimed compounds are completely different from those attributed to them by the reference description, under *In re Wilder,* Wood et al. does not anticipate the claims pending.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

(21) Claims 39-44 were rejected under 35 U.S.C. 102(b) as being anticipated by Valenzuela et al. (WO 00/11015, see pages 1-2, 115-118, 167-168, 171-176, 183-184, 207-209 and pages 68-70 of the sequence listing), as evidenced by the attached alignment 'E'."

The publication date of the Valenzuela et al. reference (WO 00/11015) is March 2, 2000. The rejections based on Valenzuela et al. under 35 U.S.C. 102(b) are believed to be moot as all claims pending in this application, as presented above, are entitled to the February 11, 2000 priority date which pre-dates the Valenzuela et al. reference.

Accordingly, the Examiner is respectfully requested to reconsider and withdraw the present rejection.

(23) Claims 39 and 43 were rejected under 35 U.S.C. 103(a) as being unpatentable over Valenzuela (WO 00/11015; published March 2, 2000) in view of Ramakrishnan (U.S.P.N 5,817,310).

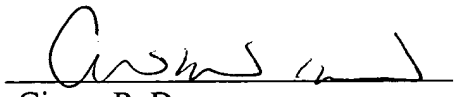
As presented above, claims 39 and 43 are entitled to the February 11, 2000 effective filing date. As discussed above, the Valenzuela reference is not prior art since it is published after the effective filing date for the claims. Since U.S.P.N 5,817,310 is a secondary reference and additionally, does not disclose specific antibodies to SEQ ID NO: 96, this rejection falls.

Accordingly, Applicants submit that claims 39 and 43 are not obvious over Valenzuela in view of U.S.P.N 5,817,310 and request that this rejection be withdrawn.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 08-1641 (Attorney Docket No.: 39780-1618P2C34). Please direct any calls in connection with this application to the undersigned at the number provided below.

Respectfully submitted,

Date: March 24, 2003



Ginger R. Dreger
Reg. No. 33,055

HELLER EHRMAN WHITE & McAULIFFE LLP
Customer No. 35489
275 Middlefield Road
Menlo Park, California 94025
Telephone: (650) 324-7000
Facsimile: (650) 324-0638

SV 423943 v1
3/21/03 1:19 PM (39780.1618)

"A"

RESULT 1
THHUB
thrombomodulin precursor [validated] - human
C;Species: Homo sapiens (man)
C;Date: 31-Dec-1988 #sequence_revision 12-May-1995 #text_change 15-Sep-2000
C;Accession: A41442; A28307; A29680; A27073; JX0264; S38954
R;Shirai, T.; Shiojiri, S.; Ito, H.; Yamamoto, S.; Kusumoto, H.; Deyashiki, Y.; Maruy
J. Biochem. 103, 281-285, 1988
A;Title: Gene structure of human thrombomodulin, a cofactor for thrombin-catalyzed ac
A;Reference number: A41442; MUID:88227901
A;Accession: A41442
A;Molecule type: DNA
A;Residues: 1-575 <SHI>
A;Cross-references: DDBJ:D00210; NID:g220126; PIDN:BAA00149.1; PID:g220127
R;Jackman, R.W.; Beeler, D.L.; Fritze, L.; Soff, G.; Rosenberg, R.D.
Proc. Natl. Acad. Sci. U.S.A. 84, 6425-6429, 1987
A;Title: Human thrombomodulin gene is intron depleted: nucleic acid sequences of the
A;Reference number: A28307; MUID:87317665
A;Accession: A28307
A;Molecule type: DNA; mRNA
A;Residues: 1-472,'A',474-575 <JAC>
A;Cross-references: GB:J02973; NID:g339658; PIDN:AAA61175.1; PID:g339659
R;Suzuki, K.; Kusumoto, H.; Deyashiki, Y.; Nishioka, J.; Maruyama, I.; Zushi, M.; Kaw
EMBO J. 6, 1891-1897, 1987
A;Title: Structure and expression of human thrombomodulin, a thrombin receptor on end
A;Reference number: A29680; MUID:88004395
A;Accession: A29680
A;Molecule type: mRNA
A;Residues: 1-575 <SUZ>
A;Cross-references: GB:X05495; NID:g37123; PIDN:CAA29045.1; PID:g736251
A;Experimental source: lung endothelium
A;Note: part of this sequence, including the amino end of the mature protein, were de
R;Wen, D.; Dittman, W.A.; Ye, R.D.; Deaven, L.L.; Majerus, P.W.; Sadler, J.E.
Biochemistry 26, 4350-4357, 1987
A;Title: Human thrombomodulin: complete cDNA sequence and chromosome localization of
A;Reference number: A27073; MUID:88024950
A;Accession: A27073
A;Molecule type: mRNA
A;Residues: 1-472,'A',474-575 <WEN>
A;Cross-references: GB:M16552; NID:g339656; PIDN:AAB59508.1; PID:g339657
A;Experimental source: placenta
A;Note: parts of this sequence were determined by protein sequencing
R;Yamamoto, S.; Mizoguchi, T.; Tamaki, T.; Ohkuchi, M.; Kimura, S.; Aoki, N.
J. Biochem. 113, 433-440, 1993
A;Title: Urinary thrombomodulin, its isolation and characterization.
A;Reference number: JX0264; MUID:93293792
A;Accession: JX0264
A;Molecule type: protein; mRNA
A;Residues: 19-472,'A',474-486 <YAM>
A;Experimental source: urine
A;Note: the urinary form appears to be identical with that circulating in plasma
R;Gerlitz, B.; Hassell, T.; Vlahos, C.J.; Parkinson, J.F.; Bang, N.U.; Grinnell, B.W.
Eur. J. Biochem. 295, 131-140, 1993
A;Title: Identification of the predominant glycosaminoglycan-attachment site in soluble
serine.
A;Reference number: S38954; MUID:94029900
A;Accession: S38954
A;Molecule type: protein
A;Residues: 475-491,'X',493-494 <GER>
A;Note: the residue designated 'X' was determined to be a Ser with covalently bound chor
R;Meininger, D.P.; Komives, E.A.
submitted to the Brookhaven Protein Data Bank, September 1995
A;Reference number: A67369; PDB:1ZAQ
A;Contents: annotation; conformation and disulfide bond assignments by (1)H-NMR, residue
R;Tulinsky, A.; Mathews, I.I.
submitted to the Brookhaven Protein Data Bank, August 1994
A;Reference number: A52804; PDB:1HLT
A;Contents: annotation; X-ray crystallography, 3.0 angstroms, residues 426-442
R;Hrabal, R.; Komives, E.A.; Ni, F.
submitted to the Brookhaven Protein Data Bank, November 1995
A;Reference number: A65583; PDB:1FGD
A;Contents: annotation; conformation by (1)H-NMR, residues 427-444
R;Hrabal, R.; Komives, E.A.; Ni, F.
Protein Sci. 5, 195-203, 1996
A;Title: Structural resiliency of an EGF-like subdomain bound to its target protein, th
A;Reference number: A58595; MUID:96276211
A;Contents: annotation; conformation by (1)H-NMR
C;Genetics:
A;Gene: GDB:THBD
A;Cross-references: GDB:119613; OMIM:188040
A;Map position: 20p11.2-20p11.2
A;Introns: #status absent
C;Complex: homodimer, urinary form
C;Function:
A;Description: inhibits thrombin activation of fibrinogen; cofactor for thrombin activa
A;Pathway: blood coagulation moderation
A;Note: the membrane-bound form is located on the endothelium luminal surface of arteri
A;Note: thrombin complexed with the membrane-bound form is subject to endocytosis
C;Superfamily: thrombomodulin; C-type lectin homology; EGF homology
C;Keywords: anticoagulant; beta-hydroxyasparagine; beta-hydroxyaspartic acid; blood coa
e protein
F;1-18/Domain: signal sequence #status predicted <SIG>
F;19-575/Product: thrombomodulin, membrane-bound form #status predicted <MAT>
F;19-513/Domain: extracellular #status predicted <EXT>
F;19-486/Product: thrombomodulin, urinary form #status experimental <MAU>
F;24-167/Domain: C-type lectin homology <LCH>
F;177-199/Region: PEST sequence
F;201-233/Region: PEST sequence
F;245-280/Domain: EGF homology <EG1>
F;288-323/Domain: EGF homology <EG2>
F;329-362/Domain: EGF homology <EG3>
F;369-404/Domain: EGF homology <EG4>
F;408-439/Domain: EGF homology <EG5>
F;445-480/Domain: EGF homology <EG6>
F;485-513/Region: PEST sequence
F;517-539/Domain: transmembrane #status predicted <TMN>
F;540-575/Domain: intracellular #status predicted <INT>
F;47,115,116,382,409/Binding site: carbohydrate (Asn) (covalent) #status predicted
F;174,225,411,504/Binding site: carbohydrate (Thr) (covalent) #status predicted
F;245-256,252-265,267-280,288-296,292-308,310-323,329-340,336-349,351-362,369-378,374-3
F;334,498/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;342/Modified site: erythro-beta-hydroxyasparagine (Asn) #status experimental
F;490,492/Binding site: chondroitin sulfate (Ser) (covalent) (partial) #status experime

Query Match 8.7%; Score 227; DB 1; Length 575;
Best Local Similarity 25.7%; Pred. No. 2.2e-08;
Matches 85; Conservative 36; Mismatches 120; Indels 90; Gaps 18;

```
Qy    16 PGPGGGEHPTADRAGCSASGACYSLHHATMKRQAAEEACILRGGALSTVRAGAELRAVLA 75
Db    23 PQPGGSQCVEHD---------CFALYPGPATFLNASQICDGLRGHLMTVRSSVAADVISL 73

Qy    76 LLRAGPGPGGGSKDLLFWVALE--------RRRSHCTLENEPLRGFSWLSSDPGGLESDT 127
Db    74 LLN---GDGGVGRRRL-WIGLQLPPGCGDPKRLG-------PLRGFQWVTGDNNTSYS-- 120

Qy   128 LQWVEEPQRS-------CTARRCAVLQATGGVEPAGWKEMRCHLRANGYLCKYQFEVLCP 180
Db   121 -RWARLDLNGAPLCGPLCVAVSAA--EATVPSEPI-WEEQQCEVKADGFLCEFHFPATCR 176

Qy   181 --APRPGAAS---NLSYRAPFQLHSAALDFSPPGTEVSALCRGQLPISVTCIAD------ 229
Db   177 PLAVEPGAAAAAVSITYGTPFAARGADFQALPVGSSAAV---APLGLQLMCTAPPGAVQG 233

Qy   230 ----EIGARWD----------KLSGDVLCPCP--------GRYLRAG---KCAEL-- 259
Db   234 HWAREAPGAWDCSVENGGCEHACNAIPGAPRCQCPAGAALQADGRSCTASATQSCNDLCE 293

Qy   260 ----PNCLDDLGGFACECATGFELGKDGRSC 286
Db   294 HFCVPN-PDQPGSYSCMCETGYRLAADQHRC 323
```

"B"

```
RESULT   1
THHUB
thrombomodulin precursor [validated] - human
C;Species: Homo sapiens (man)
C;Date: 31-Dec-1988 #sequence_revision 12-May-1995 #text_change 15-Sep-2000
C;Accession: A41442; A28307; A29680; A27073; JX0264; S38954
R;Shirai, T.; Shiojiri, S.; Ito, H.; Yamamoto, S.; Kusumoto, H.; Deyashiki, Y.; Maruy
J. Biochem. 103, 281-285, 1988
A;Title: Gene structure of human thrombomodulin, a cofactor for thrombin-catalyzed ac
A;Reference number: A41442; MUID:88227901
A;Accession: A41442
A;Molecule type: DNA
A;Residues: 1-575 <SHI>
A;Cross-references: DDBJ:D00210; NID:g220126; PIDN:BAA00149.1; PID:g220127
R;Jackman, R.W.; Beeler, D.L.; Fritze, L.; Soff, G.; Rosenberg, R.D.
Proc. Natl. Acad. Sci. U.S.A. 84, 6425-6429, 1987
A;Title: Human thrombomodulin gene is intron depleted: nucleic acid sequences of the
A;Reference number: A28307; MUID:87317665
A;Accession: A28307
A;Molecule type: DNA; mRNA
A;Residues: 1-472,'A',474-575 <JAC>
A;Cross-references: GB:J02973; NID:g339658; PIDN:AAA61175.1; PID:g339659
R;Suzuki, K.; Kusumoto, H.; Deyashiki, Y.; Nishioka, J.; Maruyama, I.; Zushi, M.; Kaw
EMBO J. 6, 1891-1897, 1987
A;T[illegible]e: Structure and expression of human thrombomodulin, a thrombin receptor on end
A;R[illegible]ence number: A29680; MUID:88004395
A;Accession: A29680
A;Molecule type: mRNA
A;Residues: 1-575 <SUZ>
A;Cross-references: GB:X05495; NID:g37123; PIDN:CAA29045.1; PID:g736251
A;Experimental source: lung endothelium
A;Note: part of this sequence, including the amino end of the mature protein, were de
R;Wen, D.; Dittman, W.A.; Ye, R.D.; Deaven, L.L.; Majerus, P.W.; Sadler, J.E.
Biochemistry 26, 4350-4357, 1987
A;Title: Human thrombomodulin: complete cDNA sequence and chromosome localization of
A;Reference number: A27073; MUID:88024950
A;Accession: A27073
A;Molecule type: mRNA
A;Residues: 1-472,'A',474-575 <WEN>
A;Cross-references: GB:M16552; NID:g339656; PIDN:AAB59508.1; PID:g339657
A;Experimental source: placenta
A;Note: parts of this sequence were determined by protein sequencing
R;Yamamoto, S.; Mizoguchi, T.; Tamaki, T.; Ohkuchi, M.; Kimura, S.; Aoki, N.
J. Biochem. 113, 433-440, 1993
A;Title: Urinary thrombomodulin, its isolation and characterization.
A;Reference number: JX0264; MUID:93293792
A;Accession: JX0264
A;Molecule type: protein; mRNA
A;Residues: 19-472,'A',474-486 <YAM>
A;Experimental source: urine
A;Note: the urinary form appears to be identical with that circulating in plasma
R;Gerlitz, B.; Hassell, T.; Vlahos, C.J.; Parkinson, J.F.; Bang, N.U.; Grinnell, B.W.
B[illegible]em. J. 295, 131-140, 1993
A[illegible]le: Identification of the predominant glycosaminoglycan-attachment site in soluble
serine.
A;Reference number: S38954; MUID:94029900
A;Accession: S38954
A;Molecule type: protein
A;Residues: 475-491,'X',493-494 <GER>
A;Note: the residue designated 'X' was determined to be a Ser with covalently bound chor
R;Meininger, D.P.; Komives, E.A.
submitted to the Brookhaven Protein Data Bank, September 1995
A;Reference number: A67369; PDB:1ZAQ
A;Contents: annotation; conformation and disulfide bond assignments by (1)H-NMR, residue
R;Tulinsky, A.; Mathews, I.I.
submitted to the Brookhaven Protein Data Bank, August 1994
A;Reference number: A52804; PDB:1HLT
A;Contents: annotation; X-ray crystallography, 3.0 angstroms, residues 426-442

R;Hrabal, R.; Komives, E.A.; Ni, F.
submitted to the Brookhaven Protein Data Bank, November 1995
A;Reference number: A65583; PDB:1FGD
A;Contents: annotation; conformation by (1)H-NMR, residues 427-444
R;Hrabal, R.; Komives, E.A.; Ni, F.
Protein Sci. 5, 195-203, 1996
A;Title: Structural resiliency of an EGF-like subdomain bound to its target protein, thr
A;Reference number: A58595; MUID:96276211
A;Contents: annotation; conformation by (1)H-NMR
C;Genetics:
A;Gene: GDB:THBD
A;Cross-references: GDB:119613; OMIM:188040
A;Map position: 20p11.2-20p11.2
A;Introns: #status absent
C;Complex: homodimer, urinary form
C;Function:
A;Description: inhibits thrombin activation of fibrinogen; cofactor for thrombin activa
A;Pathway: blood coagulation moderation
A;Note: the membrane-bound form is located on the endothelium luminal surface of arteri
A;Note: thrombin complexed with the membrane-bound form is subject to endocytosis
C;Superfamily: thrombomodulin; C-type lectin homology; EGF homology
C;Keywords: anticoagulant; beta-hydroxyasparagine; beta-hydroxyaspartic acid; blood coa
e protein
F;1-18/Domain: signal sequence #status predicted <SIG>
F;19-575/Product: thrombomodulin, membrane-bound form #status predicted <MAT>
F;19-513/Domain: extracellular #status predicted <EXT>
F;19-486/Product: thrombomodulin, urinary form #status experimental <MAU>
F;24-167/Domain: C-type lectin homology <LCH>
F;177-199/Region: PEST sequence
F;201-233/Region: PEST sequence
F;245-280/Domain: EGF homology <EG1>
F;288-323/Domain: EGF homology <EG2>
F;329-362/Domain: EGF homology <EG3>
F;369-404/Domain: EGF homology <EG4>
F;408-439/Domain: EGF homology <EG5>
F;445-480/Domain: EGF homology <EG6>
F;485-513/Region: PEST sequence
F;517-539/Domain: transmembrane #status predicted <TMN>
F;540-575/Domain: intracellular #status predicted <INT>
F;47,115,116,382,409/Binding site: carbohydrate (Asn) (covalent) #status predicted
F;174,225,411,504/Binding site: carbohydrate (Thr) (covalent) #status predicted
F;245-256,252-265,267-280,288-296,292-308,310-323,329-340,336-349,351-362,369-378,374-3
F;334,498/Binding site: carbohydrate (Ser) (covalent) #status predicted
F;342/Modified site: erythro-beta-hydroxyasparagine (Asn) #status experimental
F;490,492/Binding site: chondroitin sulfate (Ser) (covalent) (partial) #status experime

  Query Match             10.9%;  Score 222;  DB 1;  Length 575;
  Best Local Similarity   25.5%;  Pred. No. 9.2e-09;
  Matches   84;  Conservative   36;  Mismatches  119;  Indels   90;  Gaps   18;

Qy       2 PGGGEHPTADRAGCSASGACYSLHHATMKRQAAEEACILRGGALSTVRAGAELRAVLALL 61
           |||:  |        |::|:       | : |    | | |||:      :  ||
Db      25 PGGSQCVEHD---------CFALYPGPATFLNASQICDGLRGHLMTVRSSVAADVISLLL 75

Qy      62 RAGPGPGGGSKDLLFWVALE--------RRRSHCTLENEPLRGFSWLSSDPGGLESDTLQ 113
             | ||  :  | |: |:         :|          ||||| |:: |     |   :
Db      76 N---GDGGVGRRRL-WIGLQLPPGCGDPKRLG-------PLRGFQWVTGDNNTSYS---R 121

Qy     114 WVEEPQRS-------CTARRCAVLQATGGVEPAGWKEMRCHLRANGYLCKYQFEVLCP-- 164
           |              | |   |  :||   ||  |:| :| ::|:|:||:: |   |
Db     122 WARLDLNGAPLCGPLCVAVSAA--EATVPSEPI-WEEQQCEVKADGFLCEFHFPATCRPL 178

Qy     165 APRPGAAS---NLSYRAPFQLHSAALDFSPPGTEVSALCRGQLPISVTCIAD-------- 213
           |  ||||:   :::|  ||    |     | |:  :      | : : | |
Db     179 AVEPGAAAAAVSITYGTPFAARGADFQALPVGSSAAV---APLGLQLMCTAPPGAVQGHW 235

Qy     214 --EIGARWD-------------KLSGDVLCPCP--------GRYLRAG---KCAEL---- 243
             |    ||             : |   | ||         ||    |     | :|
Db     236 AREAPGAWDCSVENGGCEHACNAIPGAPRCQCPAGAALQADGRSCTASATQSCNDLCEHF 295

Qy     244 --PNCLDDLGGFACECATGFELGKDGRSC 270
             ||  |  | ::| | ||: |   |    |
Db     296 CVPN-PDQPGSYSCMCETGYRLAADQHRC 323
```

"C"

```
RESULT   1
US-08-751-305-2
; Sequence 2, Application US/08751305
; Patent No. 5965439
;  GENERAL INFORMATION:
;    APPLICANT:  Tenner et al., Andrea J.
;    TITLE OF INVENTION:  HOST DEFENSE ENHANCEMENT
;    NUMBER OF SEQUENCES:  33
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Fish & Richardson P.C.
;      STREET:  4225 Executive Square, Suite 1400
;      CITY:  La Jolla
;      STATE:  CA
;      COUNTRY:  USA
;      ZIP:  92037
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.30
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/751,305
;      FILING DATE:  18-NOV-1996
;      CLASSIFICATION:  514
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Wetherell, Jr., John R.
;      REGISTRATION NUMBER:  31,678
;      REFERENCE/DOCKET NUMBER:  07306/012001
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  619/678-5070
;      TELEFAX:  619/678-5099
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  652 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-751-305-2


  Query Match           11.8%;  Score 307;  DB 2;  Length 652;
  Best Local Similarity  21.4%;  Pred. No. 2.4e-17;
  Matches  139;  Conservative   81;  Mismatches  206;  Indels  224;  Gaps   28;

Qy       1 MRPAFALCLLWQALWPGPGGGEHPTADRAGCSASGACYSLHHATMKRQAAEEACILRGGA 60
           |  :  | ||   |   || |     :   |  : |||: |   :    |:  |   ||
Db       1 MATSMGLLLLLLLLLTQPGAGTGADTEAVVCVGT-ACYTAHSGKLSAAEAQNHCNQNGGN 59

Qy      61 LSTVRAGAE---LRAVLA--LLRAGPGPGGGSKDLLFWVALERRRSHCTLENEPLRGFSW 115
           |:||::  |   :: |||  | |         ||   ||: |:| :  |   : ||:||||
Db      60 LATVKSKEEAQHVQRVLAQLLRREAALTARMSK---FWIGLQREKGKCLDPSLPLKGFSW 116

Qy     116 LSSDPGGLESDTLQWVEEPQRSCTARRCA--VLQATGGVEP---AGWKEMRC------HL 164
           :    || ::    | :| : || ::||   :|  :  : |     | |  |
Db     117 VG---GGEDTPYSNWHKELRNSCISKRCVSLLLDLSQPLLPNRLPKWSEGPCGSPGSPGS 173

Qy     165 RANGYLCKYQFEVLCPAPRPGAASNLSYRAPFQLHSAALDFSPPGTEVSA---------- 214
              |::||: |: :|     |    ::|  |||  |::|:  |  :  :
Db     174 NIEGFVCKFSFKGMCRPLALGGPGQVTYTTPFQTTSSSLEAVPFASAANVACGEGDKDET 233

Qy     215 -----LCRGQLP-------ISVTCIADEIGARWD----------------------KL 238
                ||: : |           |:: : |  ::                      :|
Db     234 QSHYFLCKEKAPDVFDWGSSGPLCVSPKYGCNFNNGGCHQDCFEGGDGSFLCGCRPGFRL 293

Qy     239 SGDVL----------------------------CPCPGRY---------LRAGKCAELP 260
             |::                           | ||  |          :   :| : |
Db     294 LDDLVTCASRNPCSSSPCRGGATCVLGPHGKNYTCRCPQGYQLDSSQLDCVDVDECQDSP 353

Qy     261 ---NCLDDLGGFACECATGFE---------------------------------------- 278
              |::  ||| |||  |:|
Db     354 CAQECVNTPGGFRCECWVGYEPGGPGEGACQDVDECALGRSPCAQGCTNTDGSFHCSCEE 413

Qy     279 ----LGKDGRSC----VTSGEGQP--------------------TLGGTGVPTRRPPAT 309
               |:|| |       | | |                     |   ||     | :
Db     414 GYVLAGEDGTQCQDVDECVGPGGPLCDSLCFNTQGSFHCGCLPGWVLAPNGVSCTMGPVS 473

Qy     310 ATSPVPQRTWPIRVD--EKLGETPLVPEQDNSVTSIP-EIPRWGSQSTMSTLQMSLQAES 366
             |      |   || | |  ||    : |: |   |    ::| :| : || :::
Db     474 LGPPSGP---PDEEDKGEKEGST--VP---RAATASPTRGPEGTPKATPTTSRPSLSSDA 525

Qy     367 KAT------ITPSGS-------VISKFNSTTSSATPQAFDSSSA------------VVFI 401
             |       : ||||         |    : :    |   ||| |             ::|
Db     526 PITSAPLKMLAPSGSSGVWREPSIHHATAASGPQEPAGGDSSVATQNNDGTDGQKLLLFY 585

Qy     402 FVSTAVVVLVILTMTVLGLVKLCFHESPSSQPRKESMGPPGLESDPEPAA 451
             : | | :|::| :  |||  | : :  : :  |:        |  |: ||
Db     586 ILGTVVAILLLLAL-ALGL--LVYRKRRAKREEKK-------EKKPQNAA 625
```

"D"

```
RESULT   1
AAY13360
ID   AAY13360 standard; Protein; 490 AA.
XX
AC   AAY13360;
XX
DT   25-JUN-1999  (first entry)
XX
DE   Amino acid sequence of protein PRO269.
XX
KW   Secreted protein; transmembrane protein; human; enterocolitis;
KW   Zollinger-Ellison syndrome; gastrointestinal ulceration;
KW   congenital microvillus atrophy; skin disease; cell growth;
KW   abnormal keratinocyte differentiation; psoriasis; epithelial cancer;
KW   Parkinson's disease; Alzheimer's disease; ALS; neuropathy;
KW   fibromodulin; dermal scarring; Usher Syndrome; Atrophia areata;
KW   anti-thrombotic; wound healing; tissue repair.
XX
OS   Homo sapiens.
XX
PN   WO9914328-A2.
XX
PD   25-MAR-1999.
XX
PF   16-SEP-1998;   98WO-US19330.

PR   25-NOV-1997;   97US-0066840.
PR   17-SEP-1997;   97US-0059113.
PR   17-SEP-1997;   97US-0059115.
PR   17-SEP-1997;   97US-0059117.
PR   17-SEP-1997;   97US-0059119.
PR   17-SEP-1997;   97US-0059121.
PR   17-SEP-1997;   97US-0059122.
PR   17-SEP-1997;   97US-0059184.
PR   18-SEP-1997;   97US-0059263.
PR   18-SEP-1997;   97US-0059266.
PR   15-OCT-1997;   97US-0062125.
PR   17-OCT-1997;   97US-0062285.
PR   17-OCT-1997;   97US-0062287.
PR   21-OCT-1997;   97US-0063486.
PR   24-OCT-1997;   97US-0062814.
PR   24-OCT-1997;   97US-0062816.
PR   24-OCT-1997;   97US-0063045.
PR   24-OCT-1997;   97US-0063120.
PR   24-OCT-1997;   97US-0063121.
PR   24-OCT-1997;   97US-0063127.
PR   24-OCT-1997;   97US-0063128.
PR   27-OCT-1997;   97US-0063329.
PR   27-OCT-1997;   97US-0063327.
PR   28-OCT-1997;   97US-0063541.
PR   28-OCT-1997;   97US-0063542.
PR   28-OCT-1997;   97US-0063544.
PR   28-OCT-1997;   97US-0063549.
PR   28-OCT-1997;   97US-0063550.
PR   28-OCT-1997;   97US-0063564.
PR   29-OCT-1997;   97US-0063435.
PR   29-OCT-1997;   97US-0063704.
PR   29-OCT-1997;   97US-0063732.
PR   29-OCT-1997;   97US-0063738.
PR   29-OCT-1997;   97US-0063734.
PR   29-OCT-1997;   97US-0064215.
PR   29-OCT-1997;   97US-0063735.
PR   31-OCT-1997;   97US-0063870.
PR   31-OCT-1997;   97US-0064103.
PR   03-NOV-1997;   97US-0064248.
PR   07-NOV-1997;   97US-0064809.
PR   12-NOV-1997;   97US-0065186.
PR   17-NOV-1997;   97US-0065846.
PR   18-NOV-1997;   97US-0065693.
PR   21-NOV-1997;   97US-0066120.
PR   21-NOV-1997;   97US-0066364.
PR   24-NOV-1997;   97US-0066772.
PR   24-NOV-1997;   97US-0066466.
PR   24-NOV-1997;   97US-0066770.
PR   24-NOV-1997;   97US-0066511.
PR   24-NOV-1997;   97US-0066453.
XX
PA   (GETH ) GENENTECH INC.
XX
PI   Chen J,  Goddard A,  Gurney AL,  Pennica D,  Wood WI,  Yuan J;
XX
DR   WPI; 1999-229533/19.
     N-PSDB; AAX52231.

PT   New isolated human genes and polypeptides used in, e.g. treatment of
PT   gastrointestinal ulceration
XX
PS   Claim 12; Fig 36; 320pp; English.
XX
CC   AAY13344-403 represent secreted and transmembrane human proteins.
CC   The cDNA sequences are obtained from cDNA libraries, prepared from
CC   fetal lung, fetal kidney, fetal brain, fetal liver and fetal retina.
CC   The encoded polypeptides have specific uses based on their homology to
CC   known polypeptides, e.g. PRO211 and PRO217 can be used for disorders
CC   associated with the preservation and maintenance of gastrointestinal
CC   mucosa and the repair of acute and chronic mucosal lesions
CC   (e.g. enterocolitis, Zollinger-Ellison syndrome, gastrointestinal
CC   ulceration and congenital microvillus atrophy), skin diseases associated
CC   with abnormal keratinocyte differentiation (e.g. psoriasis, epithelial
CC   cancers such as lung squamous cell carcinoma of the vulva and gliomas),
CC   potent effects on cell growth and development, diseases related to
CC   growth or survival of nerve cells including Parkinson's disease,
CC   Alzheimer's disease, ALS, neuropathies or cancer. PRO265 can be used as
CC   for fibromodulin, e.g. for reducing dermal scarring.  PRO264 can be used
CC   as a target for anti-tumor drugs. PRO533 may be used in the treatment
CC   of Usher Syndrome or Atrophia areata; PRO269 can be used as an
CC   anti-thrombotic agent; PRO287 polypeptides and portions may have
CC   therapeutic applications in wound healing and tissue repair; PRO317 can
CC   be used for treating problems of the kidney, uterus, endometrium, blood
CC   vessels, or related tissue, e.g. in the heart of genital tract.
XX
SQ   Sequence   490 AA;

  Query Match             100.0%;  Score 2605;  DB 20;  Length 490;
  Best Local Similarity   100.0%;  Pred. No. 8.2e-200;
  Matches  490;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy       1 MRPAFALCLLWQALWPGPGGGEHPTADRAGCSASGACYSLHHATMKRQAAEEACILRGGA 60
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 mrpafalcllwqalwpgpgggehptadragcsasgacyslhhatmkrqaaeeacilrgga 60

Qy      61 LSTVRAGAELRAVLALLRAGPGPGGGSKDLLFWVALERRRSHCTLENEPLRGFSWLSSDP 120
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 lstvragaelravlallragpgpgggskdllfwvalerrrshctleneplrgfswlssdp 120

Qy     121 GGLESDTLQWVEEPQRSCTARRCAVLQATGGVEPAGWKEMRCHLRANGYLCKYQFEVLCP 180
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 gglesdtlqwveepqrsctarrcavlqatggvepagwkemrchlrangylckyqfevlcp 180

Qy     181 APRPGAASNLSYRAPFQLHSAALDFSPPGTEVSALCRGQLPISVTCIADEIGARWDKLSG 240
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 aprpgaasnlsyrapfqlhsaaldfsppgtevsalcrgqlpisvtciadeigarwdklsg 240

Qy     241 DVLCPCPGRYLRAGKCAELPNCLDDLGGFACECATGFELGKDGRSCVTSGEGQPTLGGTG 300
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 dvlcpcpgrylragkcaelpncldd1ggfacecatgfelgkdgrscvtsgegqptlggtg 300

Qy     301 VPTRRPPATATSPVPQRTWPIRVDEKLGETPLVPEQDNSVTSIPEIPRWGSQSTMSTLQM 360
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 vptrrppatatspvpqrtwpirvdeklgetplvpeqdnsvtsipeiprwgsqstmstlqm 360

Qy     361 SLQAESKATITPSGSVISKFNSTTSSATPQAFDSSSAVVFIFVSTAVVVLVILTMTVLGL 420
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 slqaeskatitpsgsviskfnsttssatpqafdsssavvfifvstavvvlviltmtvlgl 420

Qy     421 VKLCFHESPSSQPRKESMGPPGLESDPEPAALGSSSAHCTNNGVKVGDCDLRDRAEGALL 480
           ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 vklcfhespssqprkesmgppglesdpepaalgsssahctnngvkvgdcdlrdraegall 480

Qy     481 AESPLGSSDA 490
           ||||||||||
Db     481 aesplgssda 490
```

"E"

RESULT 4
AAY95016
ID AAY95016 standard; Protein; 490 AA.
XX
AC AAY95016;
XX
DT 19-JUN-2000 (first entry)
XX
DE Human secreted protein vp15_1, SEQ ID NO:72.
XX
KW Human; secreted protein; cancer; tumour; cardiovascular disorder;
KW blood disorder; haemophilia; autoimmune disease; diabetes; inflammation;
KW infection; fungal; bacterial; viral; HIV; allergy; arthritis;
KW neurodegenerative disease; asthma; contraceptive.
XX
OS Homo sapiens.
XX
PN WO200011015-A1.
XX
PD 02-MAR-2000.
XX
[redacted]24-AUG-1999; 99WO-US19351.
XX
PR 24-AUG-1998; 98US-0097638.
PR 24-AUG-1998; 98US-0097659.
PR 09-SEP-1998; 98US-0099618.
PR 28-SEP-1998; 98US-0102092.
PR 25-NOV-1998; 98US-0109978.
PR 23-DEC-1998; 98US-0113645.
PR 23-DEC-1998; 98US-0113646.
PR 23-AUG-1999; 99US-0379246.
XX
PA (ALPH-) ALPHAGENE INC.
XX
PI Valenzuela D, Yuan O, Hoffman H, Hall J, Rapiejko P;
XX
DR WPI; 2000-224657/19.
XX
PT New secreted or transmembrane proteins and polynucleotides encoding
PT them, useful for treating neurodegenerative disorders, autoimmune
PT diseases and cancer -
XX
PS Claim 81; Page 331-332; 357pp; English.
XX
CC The invention relates to 40 human secreted proteins (AAY94981-Y95020),
CC and cDNA sequences encoding them (AAA23423-A23462). The secreted
CC proteins of the invention include those that are thought to be only
CC partially secreted, i.e., transmembrane proteins. The proteins of the
CC [redacted] invention may exhibit one or more activities selected from the following:
CC [redacted] cytokine activity; cell proliferation; differentiation; immune
CC modulation; haematopoiesis regulation; tissue growth activity;
CC activin/inhibin activity; chemotactic/chemokinetic activity; haemostatic
CC and thrombolytic activity; anti-inflammatory activity; and tumour
CC inhibition activity. The proteins may be administered to patients as
CC vaccines, and the nucleotides may be used as part of a gene therapy
CC regime. Diseases or conditions that may be treated using the proteins or
CC nucleotides of the invention include autoimmune diseases; genetic
CC disorders; haemophilia; cardiovascular diseases; cancer; bacterial,
CC fungal and viral infections, especially HIV; multiple sclerosis;
CC rheumatoid arthritis; pulmonary inflammation; Guillain-Barre syndrome;
CC insulin dependent diabetes mellitus; and allergic reactions such as
CC asthma and anaemia. They may also be used for treating wounds, burns,
CC ulcers, osteoporosis, osteoarthritis, periodontal diseases, Alzheimer's
CC disease, Parkinson's disease, Huntington's disease and amyotrophic
CC lateral sclerosis (ALS). Proteins with activin/inhibin activity may
CC additionally be useful as contraceptives. Nucleic acid sequences of the
CC invention may be used in chromosome mapping, and as a source of
CC diagnostic primers and probes. The present sequence represents one of the
CC 40 proteins of the invention.
XX
Sequence 490 AA;

Query Match 100.0%; Score 2605; DB 21; Length 490;
Best Local Similarity 100.0%; Pred. No. 8.2e-200;
Matches 490; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

```
Qy       1 MRPAFALCLLWQALWPGPGGGEHPTADRAGCSASGACYSLHHATMKRQAAEEACILRGGA 60
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db       1 mrpafalcllwqalwpgpgggehptadragcsasgacyslhhatmkrqaaeeacilrgga 60

Qy      61 LSTVRAGAELRAVLALLRAGPGPGGGSKDLLFWVALERRRSHCTLENEPLRGFSWLSSDP 120
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db      61 lstvragaelravlallragpgpgggskdllfwvalerrrshctleneplrgfswlssdp 120

Qy     121 GGLESDTLQWVEEPQRSCTARRCAVLQATGGVEPAGWKEMRCHLRANGYLCKYQFEVLCP 180
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     121 gglesdtlqwveepqrsctarrcavlqatggvepagwkemrchlrangylckyqfevlcp 180

Qy     181 APRPGAASNLSYRAPFQLHSAALDFSPPGTEVSALCRGQLPISVTCIADEIGARWDKLSG 240
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     181 aprpgaasnlsyrapfqlhsaaldfsppgtevsalcrgqlpisvtciadeigarwdklsg 240

Qy     241 DVLCPCPGRYLRAGKCAELPNCLDDLGGFACECATGFELGKDGRSCVTSGEGQPTLGGTG 300
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     241 dvlcpcpgrylragkcaelpncldd1ggfacecatgfelgkdgrscvtsgegqptlggtg 300

Qy     301 VPTRRPPATATSPVPQRTWPIRVDEKLGETPLVPEQDNSVTSIPEIPRWGSQSTMSTLQM 360
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     301 vptrrppatatspvpqrtwpirvdeklgetplvpeqdnsvtsipeiprwgsqstmstlqm 360

Qy     361 SLQAESKATITPSGSVISKFNSTTSSATPQAFDSSSAVVFIFVSTAVVVLVILTMTVLGL 420
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     361 slqaeskatitpsgsviskfnsttssatpqafdsssavvfifvstavvvlviltmtvlgl 420

Qy     421 VKLCFHESPSSQPRKESMGPPGLESDPEPAALGSSSAHCTNNGVKVGDCDLRDRAEGALL 480
          ||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||||
Db     421 vklcfhespssqprkesmgppglesdpepaalgsssahctnngvkvgdcdlrdraegall 480

Qy     481 AESPLGSSDA 490
          ||||||||||
Db     481 aesplgssda 490
```